

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition
1	BRS	L1	1482	neuropeptide adj y	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:00		0
2	BRS	L2	606	(neuropeptide adj y) same (antagonist or agonist)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:22		0
3	BRS	L3	1	tripeptide same 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:21		0
4	BRS	L4	333	neuropeptide adj y adj receptor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:02		0
5	BRS	L5	159	4 same (antagonist or agonist)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:02		0
6	BRS	L6	35	peptide same 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:03		0
7	BRS	L7	195	peptide same 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:21		0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition
8	BRS	L8	3	(neuropeptide adj y) same tripeptide	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:22		0
9	BRS	L9	6915	tripeptide	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:28		0
10	BRS	L10	120873	(pharmaceutical or therapeutic) adj composition	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:23		0
11	BRS	L11	113	9 same 10	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:24		0
12	BRS	L12	0	11 same 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:24		0
13	BRS	L13	209	trp adj arg adj tyr	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:25		0
14	BRS	L14	751	gln adj arg adj tyr	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:25		0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
15	BRS	L15	2	trp adj arg adj tic	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:25		0	
16	BRS	L16	2	tcc adj arg adj tic	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:25		0	
17	BRS	L17	0	(13 or 14 or 15 or 16) same 10	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:26		0	
18	BRS	L18	5	(13 or 14 or 15 or 16) same 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:26		0	
19	BRS	L19	54	cationized adj albumin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:27		0	
20	BRS	L20	7303	polylysine	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:28		0	
21	BRS	L21	0	tripeptide same (19 or 20) same conjugate	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:29		0	

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Error
22	BRS	L22	2	balasubramanium adj ambikaipakan.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:32		0	
23	BRS	L23	2	chance adj william.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/03 09:32		0	

FILE 'MEDLINE' ENTERED AT 09:38:39 ON 03 JUL 2003

FILE 'CAPLUS' ENTERED AT 09:38:39 ON 03 JUL 2003  
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FILE 'AGRICOLA' ENTERED AT 09:38:39 ON 03 JUL 2003

=> s neuropeptide y  
L1 46753 NEUROPEPTIDE Y

=> s l1 (p) (agonist or antagonist)  
L2 3800 L1 (P) (AGONIST OR ANTIGONIST)

=> S TRIPEPTIDE (p) l2  
L3 6 TRIPEPTIDE (P) L2

=> duplicate remove l3  
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
PROCESSING COMPLETED FOR L3  
L4 2 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)

=> d l4 1-2 ibib abs

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2000:31342 CAPLUS  
DOCUMENT NUMBER: 132:88195  
TITLE: Neuropeptide Y agonist and antagonist peptides for control of appetite, blood pressure, cardiovascular response, libido, and circadian rhythm  
INVENTOR(S): Balasubramaniam, Ambikaipakan; Chance, William T.  
PATENT ASSIGNEE(S): University of Cincinnati, USA  
SOURCE: U.S., 17 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6013633	A	20000111	US 1997-907403	19970807
US 6235718	B1	20010522	US 1999-449914	19991202
PRIORITY APPLN. INFO.:			US 1997-907403 A3	19970807

OTHER SOURCE(S): MARPAT 132:88195

AB Dipeptides and \*\*\*tripeptides\*\*\*, and methods for pharmaceutical treatment of mammals using analogs of such dipeptides and \*\*\*tripeptides\*\*\*, are provided. More specifically, the invention relates to \*\*\*tripeptides\*\*\* and their analogs, to pharmaceutical compns. contg. such dipeptides and \*\*\*tripeptides\*\*\*, and to methods of treatment of mammals using such dipeptides and \*\*\*tripeptides\*\*\*. In addn., the invention relates to methods of treatment of mammals using such dipeptides and \*\*\*tripeptides\*\*\* for control of appetite, blood pressure, cardiovascular response, libido, and circadian rhythm. The compds. of the invention are \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* receptor \*\*\*agonists\*\*\* and antagonists.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 MEDLINE DUPLICATE 1  
ACCESSION NUMBER: 1999089557 MEDLINE  
DOCUMENT NUMBER: 99089557 PubMed ID: 9874161  
TITLE: BIBP 3226 inhibition of nicotinic receptor mediated chromaffin cell secretion.  
AUTHOR: Zhang P; Zheng J; Hexum T D

CORPORATE SOURCE: Department of Pharmacology, University of Nebraska Medical Center, Omaha 68198-6260, USA.  
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, (1998 Dec 4) 302 (2-3) 121-5.  
Journal code: 1254354. ISSN: 0014-2999.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199903  
ENTRY DATE: Entered STN: 19990326  
Last Updated on STN: 19990326  
Entered Medline: 19990318

AB (R)-N 2-(diphenacetyl)-N-[(4-hydroxyphenyl)methyl]-argininamide (BIBP 3226) is a selective \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* Y1 receptor antagonist with structural similarity to the C-terminal \*\*\*tripeptide\*\*\* of \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\*. Based on this similarity we questioned whether BIBP 3226 could act as an \*\*\*agonist\*\*\*. Incubation of BIBP 3226 with bovine chromaffin cells in culture results in the inhibition of nicotinic receptor-stimulated catecholamine secretion (IC50 = 2.4 microm). The effect of BIBP 3226 is independent of \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* action since the presence of \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* in the culture medium does not alter the effect of BIBP 3226. BIBP 3226 decreased the efficacy of the nicotinic receptor \*\*\*agonist\*\*\*, 1,1-dimethyl-4-phenylpiperizinium (DMPP), but did not change its potency suggesting non-competitive inhibition. BIBP 3226 has a similar effect on nicotinic receptor-stimulated 45Ca2+ influx. BIBP 3226 does not inhibit [3H]norepinephrine release induced by high K+ and its effect is not pertussis toxin-sensitive. We conclude that not only can BIBP 3226 act as a \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* receptor antagonist in bovine chromaffin cells but also act as an \*\*\*agonist\*\*\* and inhibit catecholamine secretion.

=> d his

(FILE 'HOME' ENTERED AT 09:38:08 ON 03 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 09:38:39 ON 03 JUL 2003

L1 46753 S NEUROPEPTIDE Y  
L2 3800 S L1 (P) (AGONIST OR ANTIGONIST)  
L3 6 S TRIPEPTIDE (P) L2  
L4 2 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)

=> s l1 (P) tripeptide

L5 18 L1 (P) TRIPEPTIDE

=> duplicate remove l5

DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
PROCESSING COMPLETED FOR L5

L6 6 DUPLICATE REMOVE L5 (12 DUPLICATES REMOVED)

=> s l6 not l4

L7 4 L6 NOT L4

=> d l7 1-4 ibib abs

L7 ANSWER 1 OF 4 MEDLINE  
ACCESSION NUMBER: 2001264387 MEDLINE  
DOCUMENT NUMBER: 21255644 PubMed ID: 11356711  
TITLE: Neuropeptide Y has a central inhibitory action on the hypothalamic-pituitary-thyroid axis.  
AUTHOR: Fekete C; Kelly J; Mihaly E; Sarkar S; Rand W M; Legradi G; Emerson C H; Lechan R M  
CORPORATE SOURCE: Tupper Research Institute and Department of Medicine, Division of Endocrinology, Diabetes, Metabolism and Molecular Medicine, New England Medical Center, Boston, Massachusetts 02111, USA.  
CONTRACT NUMBER: DA-10732 (NIDA)  
DK-37021 (NIDDK)  
SOURCE: ENDOCRINOLOGY, (2001 Jun) 142 (6) 2606-13.  
Journal code: 0375040. ISSN: 0013-7227.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English

FILE SEGMENT: Abstracted Index Medicus; Priority Journals  
ENTRY MONTH: 200106  
ENTRY DATE: Entered STN: 20010625  
Last Updated on STN: 20010625  
Entered Medline: 20010621

AB Recent evidence suggests that \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY), originating in neurons in the hypothalamic arcuate nucleus, is an important mediator of the effects of leptin on the central nervous system. As these NPY neurons innervate hypophysiotropic neurons in the hypothalamic paraventricular nucleus (PVN) that produce the \*\*\*tripeptide\*\*\*, TRH, we raised the possibility that NPY may be responsible for resetting of the hypothalamic-pituitary-thyroid (HPT) axis during fasting. To test this hypothesis, the effects of intracerebroventricularly administered NPY on circulating thyroid hormone levels and proTRH messenger RNA in the PVN were studied by RIA and in situ hybridization histochemistry, respectively. NPY administration suppressed circulating levels of thyroid hormone (T(3) and T(4)) and resulted in an inappropriately normal or low TSH. These alterations were associated with a significant suppression of proTRH messenger RNA in the PVN, indicating that NPY infusion had resulted in a state of central hypothyroidism. Similar observations were made in NPY-infused animals pair fed to the vehicle-treated controls. These data are reminiscent of the effect of fasting on the thyroid axis and indicate that NPY may play a major role in the inhibition of HPT axis during fasting.

L7 ANSWER 2 OF 4 MEDLINE  
ACCESSION NUMBER: 91193701 MEDLINE  
DOCUMENT NUMBER: 91193701 PubMed ID: 2013752  
TITLE: Multicatalytic, high-Mr endopeptidase from postmortem human brain.  
AUTHOR: McDermott J R; Gibson A M; Oakley A E; Biggins J A  
CORPORATE SOURCE: Medical Research Council, Neurochemical Pathology Unit, Newcastle General Hospital, England.  
SOURCE: JOURNAL OF NEUROCHEMISTRY, (1991 May) 56 (5) 1509-17.  
Journal code: 2985190R. ISSN: 0022-3042.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199105  
ENTRY DATE: Entered STN: 19910602  
Last Updated on STN: 20000303  
Entered Medline: 19910516

AB The main high molecular weight (650K) multicatalytic endopeptidase has been purified from postmortem human cerebral cortex. As in other tissues and species, this enzyme is composed of several subunits of 24-31k and has three distinct catalytic activities, as shown by the hydrolysis of the fluorogenic \*\*\*tripeptide\*\*\* substrates glutaryl-Gly-Gly-Phe-7-amido-4-methylcoumarin, benzyloxycarboxyl-Gly-Gly-Arg-7-amido-4-methylcoumarin, and benzyloxycarboxyl-Leu-Leu-Glu-2-naphthylamide with hydrophobic (Phe), basic (Arg), and acidic (Glu) residues in the P1 position, respectively. These activities are distinguishable by their differential sensitivity to peptidase inhibitors. The enzyme hydrolysed neuropeptides at pH 7.4 at multiple sites with widely differing rates, ranging from 113 nmol/min/mg for substance-P, down to 2 nmol/min/mg for bradykinin. The enzyme also had proteinase activity as shown by the hydrolysis of casein. For the hydrolysis of the Tyr5-Gly6 bond in luteinizing hormone-releasing hormone, the Km was 0.95 mM and the specificity constant (kcat/Km) was  $4.7 \times 10^3$  M<sup>-1</sup> s<sup>-1</sup>. The bond specificity of the enzyme at neutral pH was determined by identifying the degradation products of 15 naturally occurring peptide sequences. The bonds most susceptible to hydrolysis had a hydrophobic residue at P1 and either a small (e.g., -Gly or -NH2) or hydrophobic residue at P'1. Hydrolysis of -Glu-X bonds (most notably in \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* ) and the Arg6-Arg7 bond in dynorphin peptides was also seen. Thus the three activities identified with fluorogenic substrates appear to be expressed against oligopeptides.

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1998:597891 CAPLUS  
DOCUMENT NUMBER: 130:14221  
TITLE: A new neutral protected tripeptide which inhibits the binding of NPY to rat hippocampus membranes  
AUTHOR(S): Pinori, Massimo; Di Gregorio, Giuseppina; Starace, Olivia; Marchetti, Letizia; Mizrahi, Jacques; Mascagni, Paolo  
CORPORATE SOURCE: Italfarmaco SpA, Research Centre, Milan, I-20092, Italy

SOURCE: Peptides 1998, Proceedings of the European Peptide Symposium, Edinburgh, Sept. 8-13, 1998 (1998), Meeting Date 1996, 725-726. Editor(s): Ramage, Robert; Epton, Roger. Mayflower Scientific: Kingswinford, UK.  
CODEN: 66RCA5

DOCUMENT TYPE: Conference  
LANGUAGE: English

AB A symposium report on the prepn. and receptor binding of Nin-formyl-D-tryptophan tri- and tetrapeptide derivs. Thus, Me2CHCH2O2C-D-Trp(CHO)-Gly-Gly-NH2 showed binding to cortex (Y1) and hippocampus (Y2) receptors with IC50 = 540 and 4 nM, resp.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:497541 CAPLUS

DOCUMENT NUMBER: 129:270986

TITLE: WRYamide, a NPY-based tripeptide that antagonizes feeding in rats

AUTHOR(S): Chance, William T.; Tao, Zhiyong; Sheriff, Sulaiman; Balasubramaniam, Ambikaipakan

CORPORATE SOURCE: Department of Surgery, University of Cincinnati Medical Center, Cincinnati, OH, 45267, USA

SOURCE: Brain Research (1998), 803(1,2), 39-43

CODEN: BRREAP; ISSN: 0006-8993

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Modifications of (D-Trp32) neuropeptide Y (NPY) led to the development of potential peptide-based lower mol. wt. (500-800 Da) NPY feeding antagonists. One compd., WRYamide (N-Ac-Trp-Arg-Tyr-NH2), blocked NPY-induced feeding for 1 to 4 h when injected intrahypothalamically (i.h.t.) at 1 to 40 .mu.g. Schedule-induced feeding was also antagonized for up to 24 h by 20 .mu.g of WRYamide, i.h.t. Injection of 2.5 mg/kg (1 mg/rat) of WRYamide, i.v., also reduced significantly schedule-induced feeding for 4 h. A conditioned taste aversion could not be classically conditioned to saccharin using WRYamide as the unconditioned stimulus. These results may lead to the development of systemically active anti-obesity drugs.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 09:38:08 ON 03 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 09:38:39 ON 03 JUL 2003

L1 46753 S NEUROPEPTIDE Y  
L2 3800 S L1 (P) (AGONIST OR ANTIGONIST)  
L3 6 S TRIPEPTIDE (P) L2  
L4 2 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)  
L5 18 S L1 (P) TRIPEPTIDE  
L6 6 DUPLICATE REMOVE L5 (12 DUPLICATES REMOVED)  
L7 4 S L6 NOT L4

=> s trp-arg-tyr

L8 33 TRP-ARG-TYR

=> s gln-arg-tyr or trp-arg-tic or tcc-arg-tic

L9 117 GLN-ARG-TYR OR TRP-ARG-TIC OR TCC-ARG-TIC

=> s (l8 otr l9) (p) l1

MISSING OPERATOR L8 OTR

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s (l8 or l9) (p) l1

L10 73 (L8 OR L9) (P) L1

=> duplicate remove l10

DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L10

L11 26 DUPLICATE REMOVE L10 (47 DUPLICATES REMOVED)



=> s l11 not (l4 or l7)  
L12 26 L11 NOT (L4 OR L7)

=> d l12 1-26 ibib abs

L12 ANSWER 1 OF 26 MEDLINE  
ACCESSION NUMBER: 2001409723 MEDLINE  
DOCUMENT NUMBER: 21184972 PubMed ID: 11287086  
TITLE: Characterization and distribution of neuropeptide Y in the brain of a caecilian amphibian.  
AUTHOR: Ebersole T J; Conlon J M; Goetz F W; Boyd S K  
CORPORATE SOURCE: Department of Biological Sciences, University of Notre Dame, Notre Dame, IN 46556, USA.  
SOURCE: PEPTIDES, (2001 Mar) 22 (3) 325-34.  
Journal code: 8008690. ISSN: 0196-9781.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200107  
ENTRY DATE: Entered STN: 20010723  
Last Updated on STN: 20010723  
Entered Medline: 20010719

AB \*\*\*Neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY) from the brain of an amphibian from the order Gymnophiona (the caecilian, Typhlonectes natans) was characterized. We cloned a 790 base pair cDNA encoding the caecilian NPY precursor. The open reading frame consisted of 291 bases, indicating an NPY precursor of 97 amino acids. Both deduced and isolated NPY primary structures were Tyr-Pro-Ser-Lys-Pro-Asp-Asn-Pro-Gly-Glu(10)-Asp-Ala-Pro-Ala-Glu-Asp-Met-Ala-Lys-Tyr(20)-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu(30)-Ile-Thr-Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* . NH2. In caecilian brain, we observed NPY immunoreactive cells within the medial pallium, basal forebrain, preoptic area, midbrain tegmentum and trigeminal nucleus. The prevalence of preoptic and hypothalamic terminal field staining supports the hypothesis that NPY controls pituitary function in this caecilian.

L12 ANSWER 2 OF 26 MEDLINE  
ACCESSION NUMBER: 1998398379 MEDLINE  
DOCUMENT NUMBER: 98398379 PubMed ID: 9729264  
TITLE: WRYamide, a NPY-based tripeptide that antagonizes feeding in rats.  
AUTHOR: Chance W T; Tao Z; Sheriff S; Balasubramaniam A  
CORPORATE SOURCE: Department of Surgery, University of Cincinnati Medical Center, 231 Bethesda Avenue, Cincinnati, OH 45267, USA.  
CONTRACT NUMBER: GM 47122 (NIGMS)  
SOURCE: BRAIN RESEARCH, (1998 Aug 24) 803 (1-2) 39-43.  
Journal code: 0045503. ISSN: 0006-8993.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199905  
ENTRY DATE: Entered STN: 19990607  
Last Updated on STN: 19990607  
Entered Medline: 19990526

AB Modifications of (D-Trp32) \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY) led to the development of potential peptide-based lower molecular weight (500-800 Da) NPY feeding antagonists. One compound, WRYamide (N-AC- \*\*\*Trp\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH2), blocked NPY-induced feeding for 1 to 4 h when injected intrahypothalamically (i.h.t.) at 1 to 40 microgram. Schedule-induced feeding was also antagonized for up to 24 h by 20 microgram of WRYamide, i.h.t. Injection of 2.5 mg/kg (1 mg/rat) of WRYamide, i.v., also reduced significantly schedule-induced feeding for 4 h. A conditioned taste aversion could not be classically conditioned to saccharin using WRYamide as the unconditioned stimulus. These results may lead to the development of systemically active anti-obesity drugs.  
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L12 ANSWER 3 OF 26 MEDLINE  
ACCESSION NUMBER: 96018834 MEDLINE  
DOCUMENT NUMBER: 96018834 PubMed ID: 7565622  
TITLE: Structure-activity relationship of novel pentapeptide neuropeptide Y receptor antagonists is consistent with a noncontinuous epitope for ligand-receptor binding.  
AUTHOR: Daniels A J; Matthews J E; Viveros O H; Leban J J; Cory M;

CORPORATE SOURCE: Division of Pharmacology, Burroughs Wellcome Co Research Triangle Park, North Carolina 27709, USA.  
SOURCE: MOLECULAR PHARMACOLOGY, (1995 Sep) 48 (3) 425-32.  
Journal code: 0035623. ISSN: 0026-895X.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199510  
ENTRY DATE: Entered STN: 19951227  
Last Updated on STN: 19970203  
Entered Medline: 19951030

AB We report the first systematic study on short peptide structure affinity and activity for the \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY) receptor. A series of linear pentapeptides has been synthesized that display affinities in the low micromolar range toward rat brain NPY receptors. Furthermore, some of these compounds competitively antagonize the Y1-type NPY receptor-mediated increase in cytosolic Ca<sup>2+</sup> in human erythroleukemic (HEL) cells. The inactive NPY carboxyl-terminal pentapeptide (Thr-Arg-\*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub>; IC<sub>50</sub> > 100 microm) was modified by replacing threonine with an aromatic amino acid and glutamine with leucine. This resulted in a series of pentapeptides with dramatically improved affinity (IC<sub>50</sub> = 0.5-4 microm) for the rat brain receptor. The structure-affinity data suggest that these peptides may represent a noncontinuous epitope containing the amino-terminal tyrosine and the carboxyl-terminal residues Arg-35 and Tyr-36 of NPY.

L12 ANSWER 4 OF 26 MEDLINE

ACCESSION NUMBER: 93157164 MEDLINE  
DOCUMENT NUMBER: 93157164 PubMed ID: 1494498  
TITLE: Rainbow trout (Oncorhynchus mykiss) neuropeptide Y.  
AUTHOR: Barton C L; Shaw C; Halton D W; Thim L  
CORPORATE SOURCE: School of Biology, Queen's University of Belfast, Northern Ireland.  
SOURCE: PEPTIDES, (1992 Nov-Dec) 13 (6) 1159-63.  
Journal code: 8008690. ISSN: 0196-9781.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199303  
ENTRY DATE: Entered STN: 19930326  
Last Updated on STN: 19930326  
Entered Medline: 19930309

AB \*\*\*Neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY) has been isolated from brain extracts of the rainbow trout (Oncorhynchus mykiss) and subjected to structural analyses. Plasma desorption mass spectroscopy estimated the molecular mass of the purified peptide as 4303.9 Da. Automated Edman degradation unequivocally established the sequence of a 36 amino acid residue peptide as: Tyr-Pro-Pro-Lys-Pro-Glu-Asn-Pro-Gly-Glu-Asp-Ala-Pro-Pro-Glu-Glu-Ala-Lys-Tyr-Tyr-Thr-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg-\*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\*. The molecular mass calculated from this sequence (4304 Da) is consistent with that obtained by mass spectroscopy. The presence of a C-terminal amide was established by radioimmunoassay. Rainbow trout NPY is identical in primary structure to coho salmon (Oncorhynchus kisutch) pancreatic polypeptide (PP). These data may indicate that, in this group of salmonid fishes, a single member of the NPY/PP peptide family is expressed in both neurons and peripheral endocrine cells.

L12 ANSWER 5 OF 26 MEDLINE

ACCESSION NUMBER: 93092973 MEDLINE  
DOCUMENT NUMBER: 93092973 PubMed ID: 1459125  
TITLE: Characterization of peptides related to neuropeptide tyrosine and peptide tyrosine-tyrosine from the brain and gastrointestinal tract of teleost fish.  
AUTHOR: Jensen J; Conlon J M  
CORPORATE SOURCE: Department of Biomedical Sciences, Creighton University, School of Medicine, Omaha, Nebraska 68178.  
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1992 Dec 1) 210 (2) 405-10.  
Journal code: 0107600. ISSN: 0014-2956.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK  
ENTRY MONTH: 199301  
ENTRY DATE: Entered STN: 19930129  
Last Updated on STN: 19980206  
Entered Medline: 19930111

AB \*\*\*Neuropeptide\*\*\* \*\*\*Y\*\*\* was isolated from the brain of the Atlantic cod, *Gadus morhua* and its primary structure established as Tyr-Pro-Ile\*-Lys-Pro-Glu\*-Asn-Pro-Gly-Glu10-Asp-Ala-Pro-Ala-Asp\*-Glu\*-Leu\*-Ala- Lys\*-Tyr20-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu30-Ile-Thr-Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* - CONH2. Residues denoted by an asterisk are different from the corresponding sequence of human \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\*. A structurally similar peptide was isolated from the brain of the trout, *Oncorhynchus mykiss*. Trout \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* contains four substitutions (Ile3-->Val, Ala14-->Thr, Asp15-->Glu and Ser22-->Thr) compared with cod \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\*. A second peptide of the \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* family was identified in the trout brain and this component was structurally similar to peptide tyrosine-tyrosine previously isolated from frog intestine (six amino acid substitutions) and identical to a peptide isolated from the pancreas of the closely related species, *Oncorhynchus kisutch* (Coho salmon). Peptide tyrosine-tyrosine, with the same primary structure as the brain peptide, was also isolated from an extract of the trout stomach. The data indicate that a peptide analogous to mammalian \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* is present in the brain of teleost fish and a peptide analogous to mammalian peptide tyrosine-tyrosine is present in brain, gastrointestinal tissue and pancreas. We speculate, therefore, that the putative gene duplication that led to pancreatic polypeptide in the higher vertebrates took place after the time of divergence of fish and tetrapods.

L12 ANSWER 6 OF 26

MEDLINE

ACCESSION NUMBER: 92396601 MEDLINE  
DOCUMENT NUMBER: 92396601 PubMed ID: 1523163  
TITLE: Structural characterization of neuropeptide Y from the brain of the dogfish, *Scyliorhinus canicula*.  
AUTHOR: Conlon J M; Bjenning C; Hazon N  
CORPORATE SOURCE: Department of Biomedical Sciences, Creighton University School of Medicine, Omaha, NE 68178.  
SOURCE: PEPTIDES, (1992 May-Jun) 13 (3) 493-7.  
JOURNAL code: 8008690. ISSN: 0196-9781.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199210  
ENTRY DATE: Entered STN: 19921023  
Last Updated on STN: 19921023  
Entered Medline: 19921014

AB A peptide of the pancreatic polypeptide (PP) family was isolated in pure form from the brain of an elasmobranch fish, *Scyliorhinus canicula* (European common dogfish). The primary structure of the peptide was established as: Tyr-Pro-Ser-Lys-Pro-Asp-Asn-Pro-Gly-Glu10-Gly-Ala-Pro-Ala-Glu-Asp- Leu-Ala-Lys- Tyr20-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu30-Ile-Thr-Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH2. This sequence contains only two amino acid substitutions compared with pig \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY) (Gly for Asp11 and Lys for Arg19), and two substitutions (Gly for Asp11 and Leu for Met17) compared with frog NPY. The amino acid sequence of NPY from dogfish brain is appreciably different from the \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\*-related peptide previously isolated from dogfish pancreas (five amino acid substitutions). The data indicate that evolutionary pressure to conserve the complete primary structure of \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* has been very strong. It is suggested that the NPY-related peptide present in the pancreas of elasmobranch and teleost fish represents the piscine equivalent of mammalian peptide tyrosine tyrosine (PYY).

L12 ANSWER 7 OF 26

MEDLINE

ACCESSION NUMBER: 91301137 MEDLINE  
DOCUMENT NUMBER: 91301137 PubMed ID: 2070789  
TITLE: Primary structure and conformational analysis of peptide methionine-tyrosine, a peptide related to neuropeptide Y and peptide YY isolated from lamprey intestine.  
AUTHOR: Conlon J M; Bjornholm B; Jorgensen F S; Youson J H; Schwartz T W  
CORPORATE SOURCE: Regulatory Peptide Center, Creighton University School of Medicine, Omaha, NE 68178.  
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1991 Jul 15) 199 (2)

293-8.  
Journal code: 600. ISSN: 0014-2956.  
GERMANY; Federal Republic of  
Journal; Article; (JOURNAL ARTICLE)  
English  
Priority Journals  
199108  
Entered STN: 19910908  
Last Updated on STN: 19980206  
Entered Medline: 19910820

- AB A peptide belonging to the pancreatic-polypeptide-fold family of regulatory peptides has been isolated from the intestine of an Agnathan, the sea lamprey (*Petromyzon marinus*). The primary structure of the peptide (termed peptide methionine-tyrosine) was established as Met-Pro-Pro-Lys-Pro-Asp-Asn-Pro-Ser-Pro10-Asp-Ala-Ser-Pro-Glu-Leu-Ser-Lys-Tyr20-Met-Leu-Ala-Val-Arg-Asn-Tyr-Ile-Asn-Leu30-Ile-Thr-Arg-\*\*\*Gln\*\*\*-\*\*\*Arg\*\*\*-\*\*\*Tyr\*\*\*-CONH2. This sequence shows stronger structural similarity with pig \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (64%), particularly in the COOH-terminal region, than with pig peptide tyrosine--tyrosine (61%) or with pig pancreatic polypeptide (42%). Molecular modelling and dynamic simulation, based upon sequence similarity with turkey pancreatic polypeptide, indicates that the conformations of the polyproline-helix-like region (residues 1-8) and the alpha-helical region (residues 15-30) in turkey pancreatic polypeptide are conserved in peptide methionine-tyrosine, and that non-bonded interactions between these domains have preserved the overall polypeptide fold in the molecule. The substitution of the otherwise totally conserved Gly9 residue by serine in lamprey peptide methionine-tyrosine, however, results in a preferred structure in which the conformation of the beta-turn between the two helical domains (residues 9-14) is appreciably different.

L12 ANSWER 8 OF 26 MEDLINE

ACCESSION NUMBER: 91296574 MEDLINE  
DOCUMENT NUMBER: 91296574 PubMed ID: 2067973  
TITLE: Neuropeptide Y-related peptides from the pancreas of a teleostean (eel), holostean (bowfin) and elasmobranch (skate) fish.  
AUTHOR: Conlon J M; Bjenning C; Moon T W; Youson J H; Thim L  
CORPORATE SOURCE: Department of Biomedical Sciences, Creighton University School of Medicine, Omaha, NE 68178.  
SOURCE: PEPTIDES, (1991 Mar-Apr) 12 (2) 221-6.  
Journal code: 8008690. ISSN: 0196-9781.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199108  
ENTRY DATE: Entered STN: 19910901  
Last Updated on STN: 19980206  
Entered Medline: 19910814

- AB Homologous peptides belonging to the pancreatic polypeptide (PP) family were isolated from the pancreas of a teleostean fish, the American eel (*Anguilla rostrata*), an holostean fish, the bowfin (*Amia calva*) and an elasmobranch fish, the skate (*Raja rhina*), and their primary structures were determined. The peptides show stronger homology to \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\*, particularly in their COOH-terminal regions, than to peptide YY or pancreatic polypeptide and contain an alpha-amidated COOH-terminal tyrosine residue. The skate peptide Tyr-Pro-Pro-Lys-Pro-Glu-Asn-Pro-Gly-Asp10-Asp-Ala-Ala-Pro-Glu-Glu-Leu-Ala-Lys-Tyr20-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu30-Ile-Thr-Arg-\*\*\*Gln\*\*\*-\*\*\*Arg\*\*\*-\*\*\*Tyr\*\*\*-NH2 represents the first member of the PP family to be isolated from a cartilaginous fish. The primary structure of the pancreatic PP family peptide has been more strongly conserved among the phylogenetically more ancient holostean and elasmobranch fishes than among the teleosts. A comparison of the primary structures of all PP family peptides supports the hypothesis and evolution has acted to conserve features of tertiary structure in the molecules (e.g., the polyproline- and alpha-helices) rather than individual amino acid residues.

L12 ANSWER 9 OF 26 MEDLINE

ACCESSION NUMBER: 91219472 MEDLINE  
DOCUMENT NUMBER: 91219472 PubMed ID: 1673794  
TITLE: Characterization of melanotropin-release-inhibiting factor (melanostatin) from frog brain: homology with human neuropeptide Y.  
AUTHOR: Chartrel N; Conlon J M; Danger J M; Fournier A; Tonon M C;

CORPORATE SOURCE: European Institute for Peptide Research, Laboratory of Molecular Endocrinology, Centre National de la Recherche Scientifique, URA 650, Mont-Saint-Aignan, France.  
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1991 May 1) 88 (9) 3862-6.  
Journal code: 7505876. ISSN: 0027-8424.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199105  
ENTRY DATE: Entered STN: 19910623  
Last Updated on STN: 19950206  
Entered Medline: 19910531

AB A polypeptide was purified from frog brain extracts on the basis of its ability to inhibit alpha-melanotropin release from perfused frog neurointermediate lobes. Based on Edman degradation, amino acid analysis, and peptide mapping, the primary structure of this frog melanotropin-release-inhibiting factor (melanostatin) was determined to be H-Tyr-Pro-Ser-Lys-Pro-Asp-Asn-Pro-Gly-Glu-Asp-Ala-Glu-Asp-Met-Ala-Lys-Tyr-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg-  
\*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub>. Frog melanostatin belongs to the pancreatic polypeptide/ \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* /peptide YY family, and the structure of this peptide differs from that of human \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* by only one amino acid substitution in position 19. A synthetic replicate of frog melanostatin is coeluted with the native peptide on HPLC and is highly potent in inhibiting alpha-melanotropin secretion in vitro (IC<sub>50</sub> = 60 nM).

L12 ANSWER 10 OF 26 MEDLINE  
ACCESSION NUMBER: 91209266 MEDLINE  
DOCUMENT NUMBER: 91209266 PubMed ID: 2019251  
TITLE: Structural characterization and biological activity of a neuropeptide Y-related peptide from the dogfish, Scyliorhinus canicula.  
AUTHOR: Conlon J M; Balasubramaniam A; Hazon N  
CORPORATE SOURCE: Department of Biomedical Sciences, Creighton University School of Medicine, Omaha, Nebraska 68178.  
CONTRACT NUMBER: GM-38601 (NIGMS)  
SOURCE: ENDOCRINOLOGY, (1991 May) 128 (5) 2273-9.  
Journal code: 0375040. ISSN: 0013-7227.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 199105  
ENTRY DATE: Entered STN: 19910616  
Last Updated on STN: 19910616  
Entered Medline: 19910524

AB A peptide of the pancreatic polypeptide (PP) family was isolated in pure form from the pancreas of an elasmobranch fish, Scyliorhinus canicula (European common dogfish). The primary structure of the peptide was established as: Tyr-Pro-Pro-Lys-Pro-Glu-Asn-Pro-Gly-Glu<sub>10</sub>-Asp-Ala-Pro-Pro-Glu-Glu-Leu-Ala-Lys-Tyr<sub>20</sub>-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu<sub>30</sub>-Ile-Thr-Arg-  
\*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub>. This sequence contains 86% amino acid sequence homology with human \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\*, and the COOH-terminal region (residues 20-36) has been fully conserved. Bolus injection of a synthetic replicate of the peptide (0.5-4 nmol) into the celiac artery of conscious dogfish resulted in a significant (P less than 0.01) and dose-dependent increase in arterial blood pressure. A maximum rise in mean pressure (67 +/- 11% over mean basal values; n = 6) was elicited by an injection of 2 nmol peptide. Bolus injections of human \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (0.5-4 nmol) also elicited dose-dependent rises in blood pressure, and the effects produced by the dogfish and human peptides were not significantly different at any dose. The data are consistent with a physiological role for \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\*-related peptide in cardiovascular regulation in elasmobranch fish.

L12 ANSWER 11 OF 26 MEDLINE  
ACCESSION NUMBER: 85076996 MEDLINE  
DOCUMENT NUMBER: 85076996 PubMed ID: 3838090  
TITLE: Isolation and characterization of neuropeptide Y from porcine intestine.  
AUTHOR: Tatemoto K; Siimesmaa S; Jornvall H; Allen J M; Polak J M; Bloom S R; Mutt V

SOURCE: FEB 1985 JAN 17 179 (1) 181-4.  
Journal code: 00157. ISSN: 0014-5793.

PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198502  
ENTRY DATE: Entered STN: 19900320  
Last Updated on STN: 19900320  
Entered Medline: 19850214

AB The isolation and primary structure of intestinal **\*\*\*neuropeptide\*\*\***  
**\*\*\*Y\*\*\*** (NPY) is described. The peptide was purified from porcine  
intestinal extracts using a chemical assay and radioimmunoassay for NPY.  
The amino acid sequence of this peptide is: Tyr-Pro-Ser-Lys-Pro-Asp-Asn-  
Pro-Gly-Glu-Asp-Ala-Pro-Ala-Glu-Asp-Leu-Ala- Arg-Tyr-Tyr-  
Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg- **\*\*\*Gln\*\*\*** - **\*\*\*Arg\*\*\***  
- **\*\*\*Tyr\*\*\*** -NH<sub>2</sub>. This the structure of intestinal NPY is identical to  
the NPY of brain origin.

L12 ANSWER 12 OF 26 MEDLINE  
ACCESSION NUMBER: 83039395 MEDLINE  
DOCUMENT NUMBER: 83039395 PubMed ID: 6957876  
TITLE: Neuropeptide Y: complete amino acid sequence of the brain  
peptide.  
AUTHOR: Tatemoto K  
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE  
UNITED STATES OF AMERICA, (1982 Sep) 79 (18) 5485-9.  
Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198212  
ENTRY DATE: Entered STN: 19900317  
Last Updated on STN: 19900317  
Entered Medline: 19821221

AB The amino acid sequence of **\*\*\*neuropeptide\*\*\*** **\*\*\*Y\*\*\***, a  
36-residue peptide recently isolated from porcine brain, has been  
determined by using high performance liquid chromatography for separation  
of its tryptic and chymotryptic fragments and subsequent sequence analysis  
of the isolated fragments by an improved dansyl Edman subtractive  
technique. The amino acid sequence of **\*\*\*neuropeptide\*\*\*** **\*\*\*Y\*\*\***  
has been found to be: Tyr-Pro-Ser-Lys-Pro-Asp-Asn-Pro-Gly-Glu-Asp-Ala-Pro-  
Ala-Glu-Asp-Leu-Ala-Arg-Tyr -Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-  
Thr-Arg- **\*\*\*Gln\*\*\*** - **\*\*\*Arg\*\*\*** - **\*\*\*Tyr\*\*\*** -NH<sub>2</sub>.  
**\*\*\*Neuropeptide\*\*\*** **\*\*\*Y\*\*\*** has a high degree of sequence homology  
with peptide YY (70%), the newly isolated porcine intestinal peptide, and  
pancreatic polypeptide (50%). It is therefore proposed that  
**\*\*\*neuropeptide\*\*\*** **\*\*\*Y\*\*\***, peptide YY, and pancreatic polypeptide  
are members of a newly recognized peptide family.

L12 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1999:45196 CAPLUS  
DOCUMENT NUMBER: 130:95852  
TITLE: Preparation of cyclized peptide mimetics for  
stabilizing .alpha.-helix conformations  
INVENTOR(S): Kahn, Michael; Kim, Hwa-ok; Urban, Jan  
PATENT ASSIGNEE(S): Molecumetics Ltd., USA  
SOURCE: U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 548,997.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5859184	A	19990112	US 1997-846431	19970430
US 5840833	A	19981124	US 1995-548997	19951027
PRIORITY APPLN. INFO.: US 1995-548997			19951027	
OTHER SOURCE(S): MARPAT 130:95852				
GI				

AB There are disclosed .alpha.-helix mimetics and methods relating to the same for imparting or stabilizing .alpha.-helicity to a peptide or protein. In one aspect, the .alpha.-helix mimetics contain 11-14-membered rings I [R1-R5 = independently amino acid side chain moiety; w = (CH2)n, NH(CH2)p; n = 0-3, p = 0-2; X, Y = remainder of the peptide mimetic] covalently attached at the end or within the length of the peptide or protein. The .alpha.-helix mimetics render the resulting peptide or protein more stable with regard to thermal stability, as well as making the peptide or protein more resistant to proteolytic degrdn. In addn., the .alpha.-helix mimetics may be used in std. peptide synthesis protocols. Thus, backbone-cyclized peptide II (R = Ile-Thr-Arg-\*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -OH) was prepd. by std. solid-phase coupling methods using a protected alanine thioamide residue and a protected N-aminoleucine residue to introduce functionality for the cyclization. Cyclized peptide II enhanced .alpha.-helical stability, enhanced enzymic stability, and significant \*\*\*neuropeptide\*\*\* receptor binding affinity, as compared with \*\*\*neuropeptide\*\*\* analog Ac-Arg-Ala-Ala-Ala-Asn-Leu-Ile-Thr-Arg-\*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH2.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:384262 CAPLUS

DOCUMENT NUMBER: 127:5357

TITLE: Preparation of backbone-cyclized structures for imparting or stabilizing .alpha.-helices in peptides or proteins

INVENTOR(S): Kahn, Michael

PATENT ASSIGNEE(S): Molecumetics Ltd., USA

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9715589	A1	19970501	WO 1996-US17054	19961024
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5840833	A	19981124	US 1995-548997	19951027
AU 9674721	A1	19970515	AU 1996-74721	19961024
PRIORITY APPLN. INFO.:			US 1995-548997	19951027
			WO 1996-US17054	19961024

OTHER SOURCE(S): MARPAT 127:5357  
GI

/ Structure 2 in file .gra /

AB There are disclosed .alpha.-helix mimetics I (R1-R5 = independently amino acid side chain moieties; X, Y = remainder of the peptide or protein mol.) and methods relating to the same for imparting or stabilizing alpha-helicity to a peptide or protein. In one aspect, the .alpha.-helix mimetics contain twelve-membered rings covalently attached at the end or within the length of the peptide or protein. The .alpha.-helix mimetics render the resulting peptide or protein more stable with regard to thermal stability, as well as making the peptide or protein more resistant to proteolytic degrdn. In addn., the .alpha.-helix mimetics may be used in std. peptide synthesis protocols. Thus, \*\*\*neuropeptide\*\*\* (NPY) mimic I (X = Ac-Arg; R1 = R2= R3 = Me; R4 = CH2CONH2, R5 = CH2CHMe2; Y = Ile-Thr-Arg-\*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -OH) (II) was prepd. by solid-phase methods via Hg2+-promoted ring closure of an alanine thioamide, N-aminoleucine precursor. II showed enhanced .alpha.-helicity by CD, and significantly increased proteolytic stability compared to a linear analog. II also shows significant biol. activity in a [3H]-NPY assay.

L12 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1997:345970 CAPLUS



DOCUMENT NUMBER: 127:62212  
TITLE: Isolation and characterization of two neuropeptide Ys from the hypothalamus of a yellowfin tuna, *Thunnus albacares*  
AUTHOR(S): Ohishi, Takahide; Iguchi, Kazuaki; Mochizuki, Tohru; Hoshino, Minoru; Futai, Yoko; Yanaihara, Noboru  
CORPORATE SOURCE: School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka, 422, Japan  
SOURCE: Biomedical Research (1997), 18(2), 129-137  
CODEN: BRESO5; ISSN: 0388-6107  
PUBLISHER: Biomedical Research Foundation  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB High concn. of \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* -like immunoreactivity (NPY-IR) was detected in the ext. of yellowfin tuna (*T. albacares*) hypothalamus by RIA using antiserum specific to human NPY (26.1 pmol equiv. to human NPY/g tissue). This NPY-IR component was isolated from the crude exts. of tuna hypothalami. Two components, tuna NPY-I and NPY-II, were purified by gel filtration followed by reverse-phase HPLC. The structural anal. revealed that both components comprised of 36 amino acid residues with the C-terminal amide. The amino acid sequence of tuna NPY-I is H-Tyr-Pro-Pro-Lys-Pro-Glu-Asn-Pro-Gly-Glu-Asp-Ala-Pro-Pro-Glu-Leu-Ala-Lys-Tyr-Tyr-Thr-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg-\*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub> and that of tuna NPY-II is H-Tyr-Pro-Val-Lys-Pro-Glu-Asn-Pro-Gly-Glu-Asp-Ala-Pro-Pro-Ala-Glu-Leu-Ala-Lys-Tyr-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg-\*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub>. Tuna fish was contained 2 different types of NPY, NPY-I and II, with 7 residue substitutions when compared with human NPY.

L12 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:554363 CAPLUS  
DOCUMENT NUMBER: 119:154363  
TITLE: Primary structure of neuropeptide Y from brains of the American alligator (*Alligator mississippiensis*)  
AUTHOR(S): Parker, D. B.; MCRory, J. E.; Fischer, W. H.; Park, M.; Sherwood, N. M.  
CORPORATE SOURCE: Biol. Dep., Univ. Victoria, Victoria, BC, Can.  
SOURCE: Regulatory Peptides (1993), 45(3), 379-86  
CODEN: REPPDY; ISSN: 0167-0115  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The purifn. of \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY) from brains of the American alligator (*Alligator mississippiensis*) was achieved using reverse-phase high performance liq. chromatog. (HPLC). The amino acid sequence was detd. using automated Edman degradn. as Tyr-Pro-Ser-Lys-Pro-Asp-Asn-Pro-Gly-Glu-Asp-Ala-Pro-Ala-Glu-Asp-Met-Ala-Arg-Tyr-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg-\*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\*. Alligator is the first non-mammalian vertebrate to have an NPY with 100% sequence identity to human NPY. The conservation of alligator NPY suggests that serine in position 7 of chicken NPY evolved after the birds and reptiles diverged from a common Archosaurian ancestor. Furthermore, the sequence identity between alligator and human NPY suggests this sequence is the same as the ancestral amniote NPY.

L12 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:225861 CAPLUS  
DOCUMENT NUMBER: 118:225861  
TITLE: Characterization of the binding site of neuropeptide Y to the rabbit kidney receptor using multiple peptide synthesis  
AUTHOR(S): Beck-Sickinger, Annette G.; Duerr, Hansjoerg; Hoffmann, Eike; Gaida, Wolfram; Jung, Guenther  
CORPORATE SOURCE: Inst. Org. Chem., Univ. Tuebingen, Tuebingen, D-7400, Germany  
SOURCE: Biochemical Society Transactions (1992), 20(4), 847-50  
CODEN: BCSTB5; ISSN: 0300-5127  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Multiple peptide synthesis methods were used to characterize the binding domain of the \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY) receptor of the rabbit kidney. \*\*\*Neuropeptide\*\*\* \*\*\*Y\*\*\* 1-4-Ahx-25-36 (I) (Ahz = .epsilon.-amino-hexanoic acid) showed receptor affinity comparable to that of NPY. To elucidate the structural requirements for receptor recognition and biol. activity, each amino acid of I was exchanged by its D-enantiomer, glycine, and L-alanine. The results of structure-affinity studies indicated that the C-terminal tetrapeptide Arg-\*\*\*Gln\*\*\* -



position 36 an unsubstituted side chain and an arom. side chain are essential. In  
33Arg, 34Gln, and 35Arg cannot be replaced by any amino acid tested with  
the exception of homoarginine for the arginine residues. Amino acid  
substitutions in the region 1-4-Ahx-25-31 did not induce marked decreases  
in affinity.

L12 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:148025 CAPLUS

DOCUMENT NUMBER: 118:148025

TITLE: Defining structural requirements for neuropeptide Y  
receptors using truncated and conformationally  
restricted analogs

AUTHOR(S): Kirby, Dean A.; Koerber, Steven C.; Craig, A. Grey;  
Feinstein, Robert D.; Delmas, Laura; Brown, Marvin R.;  
Rivier, Jean E.

CORPORATE SOURCE: Clayton Found. Lab. Pept. Biol., Salk Inst., La Jolla,  
CA, 92037, USA

SOURCE: Journal of Medicinal Chemistry (1993), 36(3), 385-93

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB To further elucidate the min. bioactive conformation of  
\*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY), a series of truncated and  
conformationally constrained analogs were prep'd. The synthesis and  
purifn. of these peptides was achieved using routine lab. strategies and  
techniques. Parent mols. consisted of the native NPY N-terminal 1-4 and  
C-terminal 25-36 segments, having the residue 5-24 core replaced by either  
a single flexible .omega.-aminoalkanoic acid, or a more rigid Pro-Gly or  
Pro-D-Ala sequence which was expected to constrain a putative turn, and  
allow the N- and C-terminal to align. Crosslinking between residues 2 and  
27 through lactamization using side-chain length and chirality suggested  
by computer simulations, resulted in cyclopeptide I (Dpr =  
2,3-diaminopropanoic acid; R = Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\*  
-NH<sub>2</sub>), which exhibits very high affinity for the Y<sub>2</sub> receptor, yet very low  
affinity for the Y<sub>1</sub> receptor. The added constraint resulting from  
bridging in I as well as in others suggested that the combination of the  
deletion of residues 5-24 and the introduction of an internal ring  
produced exclusive selectivity for the Y<sub>2</sub> receptor with little or no loss  
of affinity. The tolerance of structural recognition was further  
demonstrated as a second ring was introduced which was expected to  
constrain the amphiphilic .alpha.-helic, resulting in the full Y<sub>2</sub> agonist  
bicyclic peptide II. Improvement of Y<sub>1</sub> binding activity was achieved only  
by including more residues in the central fold region, while allowing  
limited flexibility of the termini. Although the length of the bridge  
seemed to have little effect on binding potency, changes in the location  
of and chirality at the bridgehead resulted in analogs with different  
binding affinities. Combination of optimum structural modifications  
resulted in III (R<sub>1</sub> = His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg- \*\*\*Gln\*\*\* -  
\*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub>), an analog shortened by 25% but retaining  
comparable binding properties to that native NPY at Y<sub>1</sub> and Y<sub>2</sub> receptor  
types.

L12 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1992:152348 CAPLUS

DOCUMENT NUMBER: 116:152348

TITLE: Probing the functional conformation of neuropeptide Y  
through the design and study of cyclic analogs

AUTHOR(S): Bouvier, Marlene; Taylor, John W.

CORPORATE SOURCE: Lab. Bioorg. Chem. Biochem., Rockefeller Univ., New  
York, NY, 10021, USA

SOURCE: Journal of Medicinal Chemistry (1992), 35(6), 1145-55

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB The functional importance of the PP-fold conformation in  
\*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY) was investigated. NPY and  
N.alpha.-Ac-NPY(10-36), and corresponding cyclic analogs  
cyclo[18,22[Lys18,Asp22]-NPY (I; R = Ac, R<sub>1</sub> = Ala-Leu-Arg-His-Tyr-Ile-Asn-  
Leu-Ile-Thr-Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub>) and  
N.alpha.-Ac-cyclo[18,22-[Lys18,Asp22]-NPY(10-36) (I; R =  
H-Tyr-Pro-Ser-Lys-Pro-Asp-Asn-Pro-Gly-Glu-Asp-Ala-Pro-Ala-Glu-Asp-Leu, R<sub>1</sub>  
= same) were synthesized. Strategies for synthesis of the cyclic analogs  
included the use of the Kaiser oxime resin and a segment condensation  
approach. CD studies in phosphate buffer, pH 5.0, indicated self-assocn.

of all four peptides at low micromolar concns. Monomeric N.alpha.-Ac-NPY(10-36) showed only 13% .alpha.-helix, compared 32% .alpha.-helix for monomeric NPY, demonstrating a helix-stabilizing effect of residues 1-9 that is consistent with the PP fold. The [Lys18,Asp22] lactam bridge stabilized the helical conformation in N.alpha.-Ac-NPY(10-36) (51% .alpha.-helix), but was helix destabilizing in NPY (21% .alpha.-helix). In rat brain receptor binding assays, the cyclic and linear N.alpha.-Ac-NP(10-36) analogs were equipotent (IC50 = 13 nM for 125I-BH-NPY displacement), although the cyclic analog was twice as potent in rat vas deferens assays. NPY was more potent than its cyclic analog in the brain receptor binding assays (IC50 = 0.07 and 0.25 nM, resp.), but these peptides were equipotent in the vas deferens assay. These results support a functional role for the PP fold in NPY and correlate with the soln. conformations of the monomeric peptides.

L12 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1991:656661 CAPLUS

DOCUMENT NUMBER: 115:256661

TITLE: Preparation of human neuropeptide Y analogs as antihypertensives

INVENTOR(S): Boublik, Jaroslav H.; Rivier, Jean E. F.; Brown, Marvin R.; Scott, Neal A.

PATENT ASSIGNEE(S): Salk Institute for Biological Studies, USA; University of California, Oakland

SOURCE: U.S., 8 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent  
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5026685	A	19910625	US 1988-219596	19880715
US 5328899	A	19940712	US 1992-882923	19920512
PRIORITY APPLN. INFO.:			US 1988-219596	19880715
			US 1990-503198	19900330

OTHER SOURCE(S): MARPAT 115:256661

AB Human \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* analogs XQZ19Z20Z21Z22Z23-Leu-Z25Z26Z27Z28Z29Z30Z31Z32-Arg-Z34-Arg-Z36Y (X = H, .alpha.-Me amino acid residue, N-Me amino acid residue, desamino amino acid residue, C1-7 acyl; Q = Z17Z18, Z18 bond; Z17 = Met, Arg, Nle, Nva, Leu, Ala, D-Ala; Z18 = Ala, Ser, Ile, D-Ala, D-Ser, D-Ile; Z19 = Arg, Lys, Gln; Z20 = Tyr, Phe; Z21 = Tyr, Glu, His, Ala; Z22 = Ser, Ala, Thr, Asn, Asp; Z23 = Ala, Asp, Glu, Gln, Asn, Ser; Z25 = Arg, Gln; Z26 = His, Arg, Gln; Z27 = Phe, Tyr; Z28 = Ile, Leu, Val, Arg; Z29 = Asn, Ile; Z30 = Leu, Met, Thr, Val; Z31 = Ile, Val, Leu; Z32 = Thr, Phe; Z34 = Gln, Pro, His, Z36 = Phe, Tyr; Y = NH2, OH; one of Z27 and Z36 = Phe when Q = Z18) are prepd. as antihypertensives. Thus, H-Leu,Ala-Arg-Tyr-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH2 (I) is synthesized via solid-phase methods on a p-methylbenzhydrylamine hydrochloride resin using protected amino acids. Cleavage and deprotection is accomplished via treatment of the resin-bound protected peptide by HF. I is said to significantly lower mean arterial pressure after injection into rats.

L12 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1991:648249 CAPLUS

DOCUMENT NUMBER: 115:248249

TITLE: Systematic point mutation of high affinity analog neuropeptide Y 1-4-Ahx-25-36

AUTHOR(S): Beck-Sickinger, Annette G.; Gaida, Wolfram; Schnorrenberg, Gerd; Jung, Guenther

CORPORATE SOURCE: Inst. Org. Chem., Univ. Tuebingen, Tuebingen, D-7400, Germany

SOURCE: Pept. 1990, Proc. Eur. Pept. Symp., 21st (1991), Meeting Date 1990, 646-8. Editor(s): Giralt, Ernest; Andreu, David. ESCOM Sci. Publ.: Leiden, Neth.  
CODEN: 57HNAI

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Structural requirements for biol. activity and receptor recognition of the deletion \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* (NPY) peptide analog NPY 1-4-Ahx-25-36 (Ahx = 6-aminohexanoic acid) are examd. The C-terminal peptide Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH2 is essential for NPY receptor binding activity. NPY agonist activity of deletion NPY is much more sensitive to individual amino acid exchange (point mutation).

L12 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1990:515875 CAPLUS  
 DOCUMENT NUMBER: 113:115875  
 TITLE: Neuropeptide Y agonists and partial agonists  
 INVENTOR(S): Krstenansky, John L.  
 PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA  
 SOURCE: Eur. Pat. Appl., 12 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 355793	A2	19900228	EP 1989-115469	19890822
EP 355793	A3	19920422		
EP 355793	B1	19960710		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8906376	A	19900530	ZA 1989-6376	19890821
JP 02111794	A2	19900424	JP 1989-214292	19890822
JP 2791955	B2	19980827		
AT 140235	E	19960715	AT 1989-115469	19890822
ES 2091757	T3	19961116	ES 1989-115469	19890822
DK 8904207	A	19900227	DK 1989-4207	19890825
FI 8904006	A	19900227	FI 1989-4006	19890825
NO 8903430	A	19900227	NO 1989-3430	19890825
HU 50849	A2	19900328	HU 1989-4419	19890825
HU 204852	B	19920228		
CN 1042155	A	19900516	CN 1989-106524	19890825
AU 8940828	A1	19900301	AU 1989-40828	19890828
AU 618118	B2	19911212		
US 5395823	A	19950307	US 1993-32526	19930315

PRIORITY APPLN. INFO.:

US 1988-237591 19880826  
 US 1989-384373 19890724  
 US 1990-631755 19901221  
 US 1991-782890 19911018  
 US 1992-925546 19920805

OTHER SOURCE(S):

MARPAT 113:115875

AB Title peptides, e.g. H-Tys-Pro-Ser-Lys-Pro-Asp-Asn-Pro-Gly-Glu-Asp-Ala-Pro-Ala-Glu-X1-Leu-X2-Arg-Tyr-Tyr-X3-Ala-Leu-Arg-His-Tyr-X4-Asn-Leu-X5-Thr-Arg-X6--Arg-Tyr-R (X1 = Glu, Asp; X2, X3 = Ser, Ala; X4, X5 = Leu, Ile, Met, Nle, Val; X16 = Gln, Pro, His, Ile; R = OR1, NHR1; R1 = H, alkyl) were prepd. for treatment of hypotension, eating aversion disorders, and for treatment of disorders requiring activation of \*\*\*neuropeptide\*\*\* receptors. Thus, H-Tyr-Pro-Ser-Lys-Pro-Asp-Asn-Pro-Gly-Glu-Asp-Ala-Pro-Ala-Glu-Glu-Leu-Ser-Tyr-Tyr-Ala-Ala-Leu-Arg-His-Tyr-Leu-Asn-Leu-Leu-Thr-Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH2, prepd. using BOC-protected amino acids on p-methylbenzhydrylamine resin, acted as an agonist of \*\*\*neuropeptide\*\*\* with an IC50 of <50 nM.

L12 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1990:139838 CAPLUS  
 DOCUMENT NUMBER: 112:139838  
 TITLE: Neuropeptide Y analogs as cardiovascular and antiobesity agents  
 INVENTOR(S): Jung, Guenther; Beck, Annette; Schnorrenberg, Gerd; Gaída, Wolfram; Lang, Rudolf  
 PATENT ASSIGNEE(S): Boehringer Ingelheim K.-G., Fed. Rep. Ger.  
 SOURCE: Ger. Offen., 9 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3811193	A1	19891019	DE 1988-3811193	19880401
PRIORITY APPLN. INFO.:			DE 1988-3811193	19880401

OTHER SOURCE(S):

MARPAT 112:139838

AB R1-U-X-Y-Z-Ile-Asn-Leu-Ile-Thr-X1-W-X2-Z1-NH2 (R1 = R2CO, di- to pentapeptide deriv.; R2 = C1-7 alkyl, PhCH2; U = bond, aliph. amino acid residue; X, X1, X2 = basic amino acid residue, bond; Y = His, Trp, Phe, Tyr, bond, etc.; Z, Z1 = Tyr, Phe, His, Trp, Cys, naphthylalanyl, substituted Phe, etc.; W = Gln, Asn, Glu, Asp, etc.), \*\*\*neuropeptide\*\*\*

antioesity agents, were prep. Thus, H-Tyr-Pro-Ser-Lys-NH(CH<sub>2</sub>)<sub>2</sub>-CO-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub> was prep. by the solid-phase method using 9-fluorenylmethoxycarbonyl-protected amino acids on dimethoxyvaleroyloxybenzylamide-contg. resin. The latter at 5 .times. 10<sup>-8</sup> M/kg increased blood pressure in rats by 20 mmHg.

L12 ANSWER 24 OF 26 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1989:458358 CAPLUS

DOCUMENT NUMBER: 111:58358

TITLE: Preparation and testing of neuropeptide Y fragments and analogs thereof as calmodulin inhibitors

INVENTOR(S): Ishiguro, Tsuneo; Eguchi, Arahiko; Kato, Nobuaki; Matsuo, Toshiyuki

PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 22 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01006294	A2	19890110	JP 1987-241647	19870925
			JP 1987-27764	19870209

PRIORITY APPLN. INFO.:  
 AB \*\*\*Neuropeptide\*\*\* \*\*\*Y\*\*\* analogs R1-Xm-A-(His)n-B-Ile-C-Leu-Ile-YkR2 [I; A = Arg, Lys; B = Tyr, Phe, Trp; C = Asn, Gln; m, n, k = 0, 1; X = Leu, Ala-Leu, Ser-Ala-Leu, Tyr-Ser-Ala-Leu, etc.; Y = Thr, Thr-Arg, Thr-Arg-Gln, Thr-Arg-Gln-Arg, Thr-Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\*, etc.; R1 = H, (un)substituted alkyl, aralkyl, aryl, acyl; R2 = OH, NH<sub>2</sub>, (un)substituted alkylamino, aralkylamino, arylamino], useful as calmodulin inhibitors, were prep. Porcine \*\*\*neuropeptide\*\*\* (12-36), i.e., H-Ala-Pro-Ala-Glu-Asp-Leu-Ala-Arg-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub> (II), was prep. by the solid phase method on p-methylbenzhydrylamine resin. II in vitro inhibited the activation of phosphodiesterase by calmodulin with an IC<sub>50</sub> of 3.4 .times. 10<sup>-8</sup>M.

L12 ANSWER 25 OF 26 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:262687 BIOSIS

DOCUMENT NUMBER: PREV199799569290

TITLE: Isolation and characterization of neuropeptide Y from the brain of a Chinese snake, Dinodon rufozonatus.

AUTHOR(S): Ohishi, Takahide; Iguchi, Kazuaki; Mochizuki, Tohru; Hoshino, Minoru (1); Ji, Yong-Hua; Futai, Yoko; Yanaihara, Noboru

CORPORATE SOURCE: (1) Sch. Pharmaceutical Sci., Univ. Shizuoka, Shizuoka 422 Japan

SOURCE: Biomedical Research (Tokyo), (1997) vol. 18, No. 1, pp. 87-93.

ISSN: 0388-6107.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Attempt has been made to isolate \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* -like immunoreactive component from the crude extracts of the snake brain. The extracts were purified by gel filtration, followed by repeated reverse phase HPLC to give a single component of immunoreactivity. The sequence analysis and mass spectrometric analysis of the purified fraction revealed that this component comprised of 36 amino acid residues with the C-terminal amide. The amino acid sequence, H-Tyr-Pro-Ser-Lys-Pro-Asp-Ser-Pro-Gly-Glu-Asp-Ala-Pro-Ala-Glu-Asp-Met-Ala-Arg-Tyr-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg- \*\*\*Gln\*\*\* - \*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub>, was found to be identical to that of chicken NPY and differ in only one residue at position 7 from that of human NPY.

L12 ANSWER 26 OF 26 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 91:265949 SCISEARCH

THE GENUINE ARTICLE: FK184

TITLE: CHARACTERIZATION OF MELANOTROPIN-RELEASE-INHIBITING FACTOR (MELANOSTATIN) FROM FROG BRAIN - HOMOLOGU WITH HUMAN NEUROPEPTIDE-Y

AUTHOR: CHARTREL N; CONLON J M; DANGER J M; FOURNIER A; TONON M C; VAUDRY H (Reprint)

CORPORATE SOURCE: UNIV ROUEN HAUTE NORMANDIE, EUROPEAN INST PEPTIDE RES, MOLEC ENDOCRINOL LAB, CNRS, URA 650, INSERM, F-76134 MT ST

ALIGMAN, FRANCE UNIV QUEBEC, INST NATL RECH SCI SANTE,  
POINTE CLAIRE 1G6, QUEBEC, CANADA; CREIGHTON UNIV, SCH  
MED, DEPT BIOMED SCI, CTR REGULATORY PEPTIDE, OMAHA, NE,  
68178

COUNTRY OF AUTHOR: FRANCE; CANADA; USA  
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE  
UNITED STATES OF AMERICA, (1991) Vol. 88, No. 9, pp.  
3862-3866.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: ENGLISH  
REFERENCE COUNT: 43

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB A polypeptide was purified from frog brain extracts on the basis of its  
ability to inhibit alpha-melanotropin release from perifused frog  
neurointermediate lobes. Based on Edman degradation, amino acid analysis,  
and peptide mapping, the primary structure of this frog  
melanotropin-release-inhibiting factor (melanostatin) was determined to be  
H-Tyr-Pro-Ser-Lys-Pro-Asp-Asn-Pro-Gly-Glu-Asp-Ala-Pro-Ala-Glu-Asp-Met-Ala-  
Lys-Tyr-Tyr-Ser-Ala-Leu-Arg-His-Tyr-Ile-Asn-Leu-Ile-Thr-Arg- \*\*\*Gln\*\*\* -  
\*\*\*Arg\*\*\* - \*\*\*Tyr\*\*\* -NH<sub>2</sub>. Frog melanostatin belongs to the  
pancreatic polypeptide/ \*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* /peptide YY  
family, and the structure of this peptide differs from that of human  
\*\*\*neuropeptide\*\*\* \*\*\*Y\*\*\* by only one amino acid substitution in  
position 19. A synthetic replicate of frog melanostatin is coeluted with  
the native peptide on HPLC and is highly potent in inhibiting  
alpha-melanotropin secretion in vitro (IC<sub>50</sub> = 60 nM).

=> s polylysine or (cationized albumin)  
L13 16554 POLYLYSINE OR (CATIONIZED ALBUMIN)

=> s l13 (p) tripeptide (p) conjugate  
L14 0 L13 (P) TRIPEPTIDE (P) CONJUGATE

=> s balasubramanium a/au  
L15 2 BALASUBRAMANIAM A/AU

=> d l15 1-2 ibib abs

L15 ANSWER 1 OF 2 MEDLINE  
ACCESSION NUMBER: 84184641 MEDLINE  
DOCUMENT NUMBER: 84184641 PubMed ID: 6674212  
TITLE: Neurogenic pulmonary edema during hyperpyrexia convulsions.  
AUTHOR: Dash H H; Rattan S N; \*\*\*Balasubramanium A\*\*\* ; Gode G G  
SOURCE: INDIAN JOURNAL OF PEDIATRICS, (1983 Sep-Oct) 50 (406)  
561-4.  
Journal code: 0417442. ISSN: 0019-5456.  
PUB. COUNTRY: India  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198406  
ENTRY DATE: Entered STN: 19900319  
Last Updated on STN: 20000303  
Entered Medline: 19840608

L15 ANSWER 2 OF 2 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 87069119 EMBASE  
DOCUMENT NUMBER: 1987069119  
TITLE: Synthesis of neuropeptide Y.  
AUTHOR: \*\*\*Balasubramanium A.\*\*\* ; Grupp I.; Srivastava L.; et  
al.  
CORPORATE SOURCE: Department of Surgery, University of Cincinnati Medical  
Center, Cincinnati, OH 45267, United States  
SOURCE: International Journal of Peptide and Protein Research,  
(1987) 29/1 (78-83).  
CODEN: IJPPC3  
COUNTRY: Denmark  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 029 Clinical Biochemistry  
008 Neurology and Neurosurgery  
LANGUAGE: English

=> s chance william/au  
L16 2 CHANCE WILLIAM/AU

=> d 116 1-2 ibib abs

L16 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:661046 CAPLUS

DOCUMENT NUMBER: 130:33434

TITLE: NPY upregulates genes containing cyclic AMP response element in human neuroblastoma cell lines bearing Y1 and Y2 receptors: involvement of CREB

AUTHOR(S): Sheriff, Sulaiman; Dayal, Rameshwar; Kasckow, John; Regmi, Ajit; \*\*\*Chance, William\*\*\* ; Fischer, Josef; Balasubramaniam, Ambikaipakan

CORPORATE SOURCE: College of Medicine, Department of Surgery, University of Cincinnati, Cincinnati, OH, 45267, USA

SOURCE: Regulatory Peptides (1998), 75-76, 309-318

CODEN: REPPDY; ISSN: 0167-0115

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Four NPY receptor subtypes have been cloned, and shown to be coupled to both Ca<sup>2+</sup> and CAMP. However, very little is known about the downstream elements mediating NPY actions. It has recently been demonstrated in our lab. that intrahypothalamic (IHT) administration of NPY induces hypothalamic CaM kinase activity, CAMP response element binding protein (CREB) phosphorylation and CAMP response element (CRE) binding activity in rat hypothalamic nuclear proteins. In the present study, we have investigated whether these changes in CRE binding transcriptional factors activated by NPY results in gene regulation using a human neuroblastoma cell line (SK-N-BE2). This cell line which expresses the Y2 subtype of NPY receptors was transfected with a fusion gene contg. 1.305 kb of human CRF 5' flanking region with a perfect palindromic CRE site linked to firefly luciferase gene. NPY treatment increased CaM kinase II activity, CREB phosphorylation and CRE binding in these cells. In transfected cells, luciferase activity was also increased by NPY (1.8-4-fold) within 4 h of treatment. Moreover, forskolin (7-30-fold), which stimulates CAMP prodn., and thapsigargin (6-8-fold), which mobilizes intracellular calcium, also increased luciferase activity within 4 h of treatment. PMA (phorbol-12-myristate-13-acetate), an activator of protein kinase-C, induced luciferase activity by 1.8-fold. NPY augmented forskolin-stimulated luciferase activity from 11- to 15-fold, but had no significant effect on thapsigargin-induced luciferase activity. These findings suggest that activation of protein kinase A (PKA) or CaM kinase leads to the induction of fusion gene. NPY treatment upregulated fusion gene expression through Ca<sup>2+</sup> pathway in SK-N-BE2 cell line. Pretreatment with CREB antisense, but not the sense oligodeoxynucleotides, inhibited forskolin-, thapsigargin- and NPY-stimulated luciferase activity. However, CREB sense or antisense oligodeoxynucleotide treatment had no effect on PMA-stimulated luciferase activity. Furthermore, NPY induced CRE binding activity and the expression of CRE contg. Y1 receptor gene in SK-N-MC cell line. These findings suggest that NPY can upregulate CRE contg. reporter gene including Y1 receptor gene and NPY-induced reporter gene regulation in SK-N-BE2 cells is mediated by intracellular Ca<sup>2+</sup> and CREB protein.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1998:512644 BIOSIS

DOCUMENT NUMBER: PREV199800512644

TITLE: NPY upregulates genes containing cyclic AMP response element in human neuroblastoma cell lines bearing Y1 and Y2 receptors: Involvement of CREB.

AUTHOR(S): Sheriff, Sulaiman (1); Dayal, Rameshwar; Kasckow, John; Regmi, Ajit; \*\*\*Chance, William\*\*\* ; Fischer, Josef; Balasubramaniam, Ambikaipakan

CORPORATE SOURCE: (1) Dep. Surg., Univ. Cincinnati, Coll. Med., 231 Bethesda Ave., Cincinnati, OH 45267 USA

SOURCE: Regulatory Peptides, (Sept. 25, 1998) vol. 75-76, No. 0, pp. 309-318.

ISSN: 0167-0115.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Four NPY receptor subtypes have been cloned, and shown to be coupled to both Ca<sup>2+</sup> and CAMP. However, very little is known about the downstream elements mediating NPY actions. It has recently been demonstrated in our laboratory that intrahypothalamic (IHT) administration of NPY induces hypothalamic CaM kinase activity, cyclic AMP response element binding

protein (CREB) phosphorylation and cyclic AMP response element (CRE) binding activity in rat hypothalamic nuclear proteins. In the present study, we have investigated whether these changes in CRE binding transcriptional factors activated by NPY results in gene regulation using a human neuroblastoma cell line (SK-N-BE2). This cell line which expresses the Y2 subtype of NPY receptors was transfected with a fusion gene containing 1.305 kb of human CRF 5' flanking region with a perfect palindromic CRE site linked to firefly luciferase gene. NPY treatment increased Cam kinase II activity, CREB phosphorylation and CRE binding in these cells. In transfected cells, luciferase activity was also increased by NPY (1.8-4-fold) within 4 h of treatment. Moreover, forskolin (7-30-fold), which stimulates cAMP production, and thapsigargin (6-8-fold), which mobilizes intracellular calcium, also increased luciferase activity within 4 h of treatment. PMA (phorbol-12-myristate-13-acetate), an activator of protein kinase-C, induced luciferase activity by 1.8-fold. NPY augmented forskolin-stimulated luciferase activity from 11- to 15-fold, but had no significant effect on thapsigargin-induced luciferase activity. These findings suggest that activation of protein kinase A (PKA) or Cam kinase leads to the induction of fusion gene. NPY treatment upregulated fusion gene expression through Ca<sup>2+</sup> pathway in SK-N-BE2 cell line. Pretreatment with CREB antisense, but not the sense oligodeoxynucleotides, inhibited forskolin-, thapsigargin- and NPY-stimulated luciferase activity. However, CREB sense or antisense oligodeoxynucleotide treatment had no effect on PMA-stimulated luciferase activity. Furthermore, NPY induced CRE binding activity and the expression of CRE containing Y1 receptor gene in SK-N-MC cell line. These findings suggest that NPY can upregulate CRE containing reporter gene including Y1 receptor gene and NPY induced reporter gene regulation in SK-N-BE2 cells is mediated by intracellular Ca<sup>2+</sup> and CREB protein.

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(FILE 'HOME' ENTERED AT 09:38:08 ON 03 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 09:38:39 ON 03 JUL 2003

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L1      46753 S NEUROPEPTIDE Y
L2      3800 S L1 (P) (AGONIST OR ANTIGONIST)
L3      6 S TRIPEPTIDE (P) L2
L4      2 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5      18 S L1 (P) TRIPEPTIDE
L6      6 DUPLICATE REMOVE L5 (12 DUPLICATES REMOVED)
L7      4 S L6 NOT L4
L8      33 S TRP-ARG-TYR
L9      117 S GLN-ARG-TYR OR TRP-ARG-TIC OR TCC-ARG-TIC
L10     73 S (L8 OR L9) (P) L1
L11     26 DUPLICATE REMOVE L10 (47 DUPLICATES REMOVED)
L12     26 S L11 NOT (L4 OR L7)
L13     16554 S POLYLYSINE OR (CATIONIZED ALBUMIN)
L14     0 S L13 (P) TRIPEPTIDE (P) CONJUGATE
L15     2 S BALASUBRAMANIAM A/AU
L16     2 S CHANCE WILLIAM/AU

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=> log y

COST IN U.S. DOLLARS

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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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STN INTERNATIONAL LOGOFF AT 09:51:50 ON 03 JUL 2003